Vasculite Leucocitoclástica: Um Fenómeno Paraneoplásico Raro na Neoplasia do Ovário

Leukocytoclastic Vasculitis: A Rare Paraneoplastic Phenomenon in Ovarian Tumor

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Resumo:

A vasculite leucocitoclástica (VLC) é um processo inflamatório que afeta vasos sanguíneos de pequeno calibre, na maioria das vezes secundária a determinada patologia, mas descrições da sua associação com neoplasias sólidas são raras.

Apresentamos o caso de uma doente de 75 anos com um exantema macular eritematoso e púrpura palpável nos membros, cuja biópsia cutânea revelou VLC, como única manifestação de neoplasia do ovário diagnosticada posteriormente. Apesar da melhoria das lesões cutâneas com corticoterapia, ainda que sem resolução total, apenas o tratamento da neoplasia de base, para o qual a doente não apresentou condições clínicas, poderia resolver todo o quadro.

Apenas um caso de VLC paraneoplásica está relatado, na literatura, no contexto de neoplasia do ovário.

Palavras-chave: Neoplasias do Ovário; Síndromes Paraneoplásicos; Vasculite Leucocitoclástica Cutânea.

Abstract:

Leukocytoclastic vasculitis (LCV) is an inflammatory process of small-sized vessels, most often secondary to a specific pathology, but its association with solid malignancies is rarely described.

We report a case of a 75-year-old female patient who presented with erythematous macules and palpable purpura affecting her limbs, whose skin biopsy revealed LCV, as a solitary manifestation of a later diagnosed ovarian neoplasm. Despite the improvement of cutaneous vasculitis with corticosteroids, even without total resolution, only the treatment of the underlying malignancy, for which the patient had no clinical conditions, could resolve the entire condition.

To our knowledge only 1 case of a paraneoplastic LCV has been reported in the context of an ovarian neoplasm.

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Introduction

Leukocytoclastic vasculitis is a cutaneous, small-vessel vasculitis of the dermal capillaries and venules that can be idiopathic or associated with infections, neoplasm, autoimmune disorders or toxic exposure.[1,2] LCV has been associated more commonly with hematological rather than solid malignancies.[3] Due to the rarity of the simultaneous presentation of these conditions and the lack of a temporal association, the relationship between those two entities still remains unclear, as also the underlying mechanism. We report a rare case of paraneoplastic LCV as an initial presentation of an ovarian tumor.

Case Report

A 75-year-old Caucasian female attended to the emergency department because of subacute painful skin lesions. She presented with erythematous non-exudative periungual lesions on her hands (Fig. 1A), pruritic purpuric lesions on both thighs and extensive coalescent erythematous and exudative ulcers with central areas of apparent necrosis, with great loss of substance on both legs (Fig. 1B). The rest of the examination was irrelevant.

She reported weight loss greater than 10% in the past 4 months, without associated fever or night sweating. No other systemic symptoms were found.

Her medical history included arterial hypertension controlled with medication and permanent atrial fibrillation without hypocoagulation due to microcytic hypochromic anemia with unknown etiology. There was no recent introduction of any medication or consumption of herbal products.

The biochemical analysis revealed non-oliguric acute kidney injury (serum creatinine 3.1 mg/dL; normal range (N) 0.6-1.1 mg/dL) with sub-nephrotic proteinuria, without hematuria, metabolic acidosis or electrolyte disturbances associated; elevation of inflammatory parameters (C-reactive protein 288.20 mg/L; N < 5 mg/L - and erythrocyte sedimentation rate 103 mm/1 h; N: 0-30 mm/1 h), with no change in blood cell count,

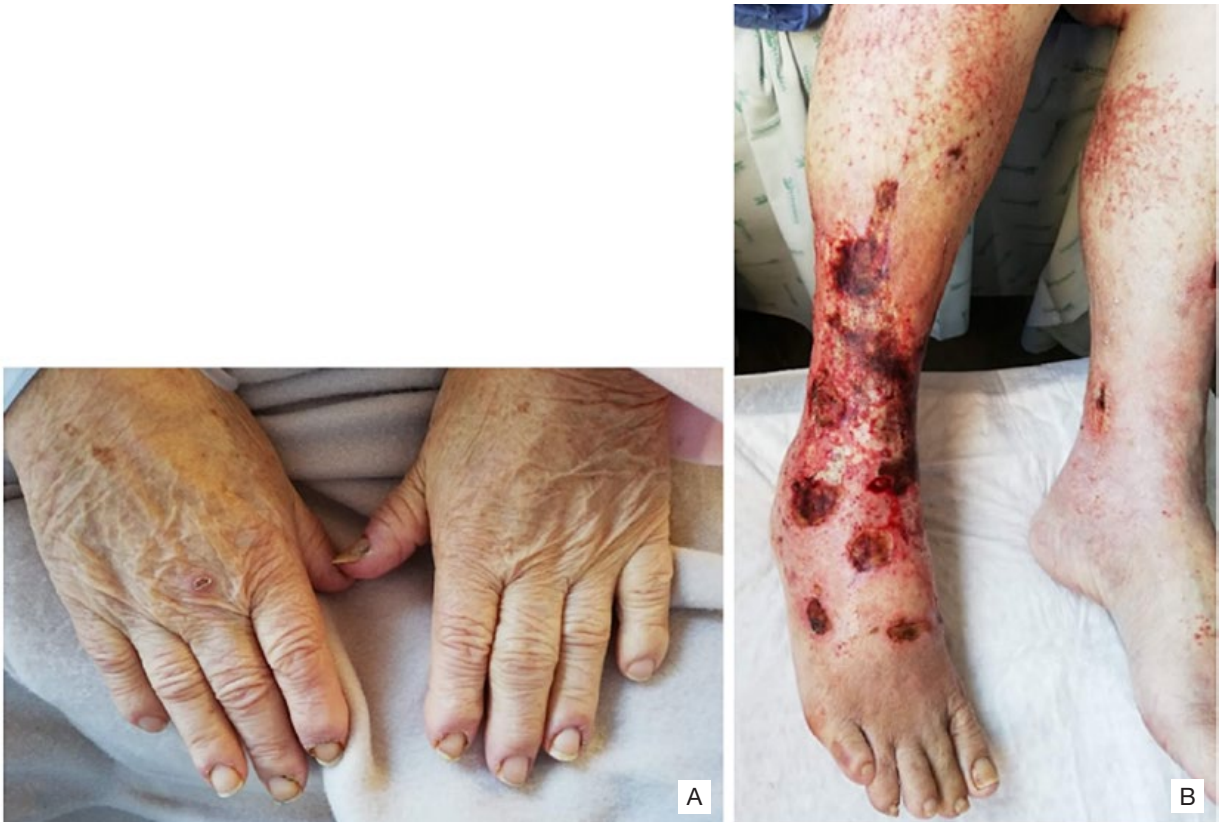

Figure 1: Showing erythematous non-exudative periungual lesions of the hands (A) and extensive coalescent erythematous ulcers with central areas of apparent necrosis more expressive in the right leg (B).

except persistent microcytic hypochromic anemia (hemoglobin 8.0 g/dL - N: 12.0-16.0 g/dL; VGM 71.8 fL – N: 80-100 fL; HGM 23.7 pg – N: 26-34 pg) with ferropenia.

A skin biopsy of a purpuric lesion on her thigh confirmed LCV involving vessels of the dermis (Fig. 2).

Additional diagnostic testing for secondary causes found negative serologies, including human immunodeficiency virus and hepatotropic viruses, and negative immunologic study (negative ANA and ANCA, normal immunoglobulin levels, no consumption of complement).

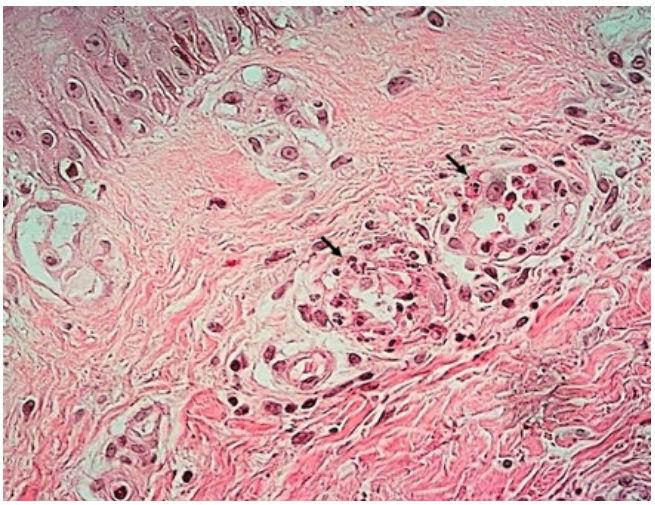

Figure 2: Histology of the cutaneous biopsy (hematoxylin and eosin staining, magnification 400x) showing, in the middle (black arrows), vasculitis lesions with aspects suggestive of neutrophil fragmentation.

A thoracic-abdominal-pelvic computed tomography (CT) scan revealed two contrast-enhanced heterogeneous lesions in pelvis, raising suspicion for neoplastic disease. Endoscopic studies were unremarkable. Due to the suspicion of a possible ovarian neoplasm an abdominal-pelvic magnetic resonance imaging was performed, showing an expansive necrotizing lesion with possible invasion of intestinal loops, associated to a cystic lesion of the left ovary. A punch biopsy revealed a malignant clear cell carcinoma, compatible with primary ovarian neoplasm (Fig. 3). The tumor markers analysis has shown a CA-125 of 40.1 UI/mL (N <35 UI/mL).

Therefore, a diagnosis of an ovarian neoplasm was made, with initial presentation as paraneoplastic phenomenon: cutaneous leukocytoclastic vasculitis and possible glomerulonephritis.

The patient started oral prednisolone 0.75 mg/kg, with gradual improvement of cutaneous vasculitis and resolution of proteinuria, with normalization of kidney function.

During hospitalization, the patient presented an extensive right deep vein thrombosis. Despite anticoagulation, with attentive surveillance of anemia worsening, reassessment angio-CT showed non-recanalization of the affected area and progression of deep vein thrombosis to the left side as well. In the

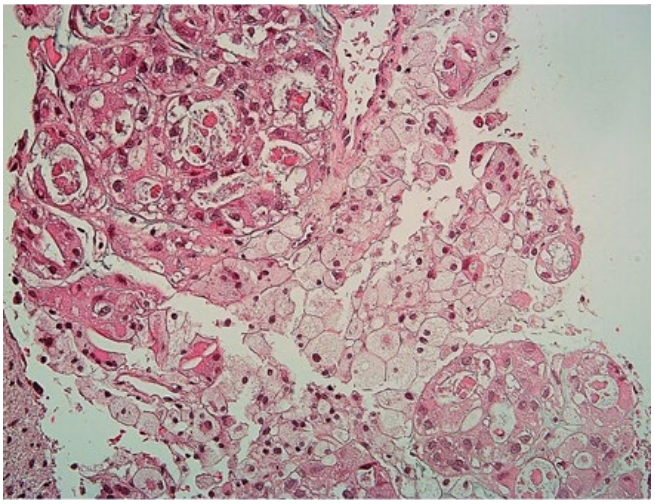

Figure 3: Histology of the adnexal lesion biopsy (hematoxylin and eosin staining, magnification 400x) showing a malignant neoplasm with morphological characteristics of clear cell carcinoma.

context of this complication and due to the poor patient status, priority was given to symptomatic support treatment, as the patient was unfit for surgery or systemic treatment, culminating in death nine months after diagnosis.

Discussion

LCV is a small-vessel vasculitis that typically features leukocytoclasia of infiltrating granulocytes with fibrinoid necrosis of the vascular wall and subsequent extravasation of erythrocytes.[1] Clinically is characterized by erythematous macules that can progress to palpable diffuse purpura.[1]

In more than two-thirds of cases a secondary process is identified, such as exposure to drugs, infection, connective tissue diseases, primary systemic vasculitis and neoplastic causes.[2]

The prevalence of malignancy in patients with LCV is unknown. Most reported cases are associated to hematological neoplasms (lymphomas and leukemias) and rarely solid tumors. The most frequently described are non-small cell lung cancer, breast, prostate, colon, renal and squamous cell carcinoma.[3] We found only one case of asymptomatic ovarian neoplasia that manifested as cutaneous vasculitis.[4] The pathological mechanism by which malignancies cause vasculitis is not fully understood but some hypotheses have been proposed, including the deposition in vessel walls of immune-complexes formed in response to tumor antigens with subsequent inflammation; cross-reaction between the host immunologic response directed at tumor antigens and the normal blood vessel antigens; and release of tumor mediators that directly induce vascular injury.[5]

The risk of internal organ involvement is not negligible.

The case reported illustrates that cutaneous vasculitis can be the solitary manifestation of ovarian neoplasm, despite significant weight loss ignored by the patient. We consider the LCV was a paraneoplastic phenomenon that allowed the diagnosis of an occult neoplasm.

Although treatment with corticosteroids improved the cutaneous vasculitis, only the treatment of underlying malignancy would probably solve the entire clinical situation.[1] However, as mentioned above, given the low Eastern Cooperative Oncology Group (ECOG) performance status, priority was given to symptomatic supportive therapy.

The authors intend, therefore, to draw attention to the rarity of this association and the importance of excluding a secondary cause, including occult malignancy, in the presence of LCV. It also highlights that, even in the absence of a cause, if LCV does not improve with corticosteroid therapy, further evaluation may be necessary. ■

Declaração de Contribuição

JM – Elaboração do artigo
RNS – Escrita e revisão do artigo
RRS – Escrita, Revisão do artigo e escolha de imagens
AS – Revisão anatomopatológica e imagem
CR – Revisão do manuscrito
Todos os autores aprovaram a versão final a ser submetida.

Contributorship Statement

JM – Preparation of the article
RNS – Writing and revision of the article
RRS – Writing, revision of the article and choice of images
AS – Anatomopathological revision and imaging
CR – Revision of the manuscript
All authors approved the final draft.

Responsabilidades Éticas

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